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REGION

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## Biological effects of extremely low radiation background conditions

Although much is known about the effects of exposure to high/medium doses of ionizing radiation, large uncertainties concerns the effects of low and extremely low doses of radiation. Phenomena like bystander effects, adaptive response or genomic instability have been typically observed at low doses, but their impact on human health is still under debate. The cellular response to extremely low doses as those related to radiation background is an even more open question. To experimentally address this scientific topic a unique opportunity is represented by the existence of deep underground laboratories, such as the Laboratoire Souterrain de Modane CNRS, France, and the Laboratori Nazionali del Gran Sasso INFN, Italy. This proposal aims to investigate the mechanisms involved in low dose radiation response of human/rodent cell cultures and radiosensitive mice (pKZ1) kept underground, in conditions of extremely low levels of background ionizing radiation, or in "reference" background radiation laboratories. A characterization of the different components of the radiation environments where the experiments will be carried out will be performed. The cell cultures will be periodically monitored for the onset of divergences in biochemical behavior (e.g., for changes of the cell cycle regulation, cell proliferation and stability of the genome, gene expression of stress response enzymes). Differences in chromosomal inversions as sign of DNA damage will be evaluated in pKZ1 mice; in addition, mRNAs and miRNAs profiling will be performed in order to better evaluate the impact of low background radiation on gene expression in vivo. Modifications in the cellular/animal response to acute stress will also be studied after exposure to chemicals or to moderate acute doses of ionizing radiation. The main outcome of the project will be determination of mechanisms regulated by low radiation doses which are necessary for physiological functioning and ability to cope with DNA damage.

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